

## REMARKS

Reconsideration of this application, as amended, is respectfully requested.

The Applicants wish to draw the Examiner's attention to the Applicants' related co-pending applications and issued patents (see Appendix A) directed to nanoparticles and methods of preparation and use thereof.

The Applicants note that the Examiner did not return executed copies of the PTO 1449 forms for the 6<sup>th</sup> Supplemental IDS that was hand delivered to the Examiner on September 9, 2002. Subsequent to the issuance of this Office action, the Applicants had filed a 7<sup>th</sup> Supp. IDS. The Applicants request that the Examiner fully execute the PTO 1449 forms for the 6<sup>th</sup> Supp. IDS, and 7<sup>th</sup> Supp. IDS and return a copy of the same to the undersigned representative. Copies of the 6<sup>th</sup> and 7<sup>th</sup> Supplemental IDSs, associated PTO 1449 forms, and PTO stamped postcards acknowledging receipt of the IDSs, PTO 1449 forms and references are attached. The Examiner is requested to contact the undersigned representative if the Examiner would like to have another copy of the references.

The specification was amended to update the priority claim. No new matter has been introduced by this amendment.

Claims 237-265 were pending in this application. Claims 237-240, 252 and 254 were amended to correct grammatical and typographical errors. New claims 433-446 were added to further clarify the invention. The new claims are supported, for example, by claims 237-265, and the specification at page 20, lines 23 to page 21, line 2; and page 69, line 26 to page 70, line 8. Thus, the amendment and new claims do not constitute new matter.

Turning to the office action, claims 237-265 stand rejected under 35 U.S.C. section 102(e) as being anticipated by, or in the alternative, under 35 USC section 103(a) as being obvious over Yguerabide (U.S. Patent No. 6,214,560)("Yguerabide"). The Applicants respectfully traverse this rejection.

The Federal Circuit has stated that for prior art to anticipate under section 102, every element of the claimed invention must be identically disclosed in a single reference. Corning Glass Works v. Sumitomo Electric, 9 U.S.P.Q.2d 1962, 1965 (Fed. Cir. 1989). The exclusion of a claimed element, no matter how insubstantial or obvious, from a reference is enough to negate anticipation. Connell v. Sears, Roebuck & Co., 220 U.S.P.Q 193, 1098 (Fed. Cir. 1983).

Likewise, the Federal Circuit reiterated the manner in which obviousness rejections are to be reviewed. Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, "a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success." *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991), citing *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q. 2d 1529, 1531 (Fed. Cir. 1988). Contrary to the Examiner's position, Yguerabide does not teach or suggest what the Applicants have done.

Specifically, the Examiner alleged that Yguerabide taught detection and measurement of one or more analytes in a sample using particles of specific composition and size using light scattering. The discussion is found starting in col. 82, line 35, of Yguerabide. Col. 83 provides further discussion regarding particle size and particle binding to a surface. Cols. 77-80 relate to particles and their preparation. Col. 110 (Example 32) relates to a nucleic acid labeled particle but does not provide or suggest any particle surface density. Furthermore, surface density cannot be calculated since Yguerabide does not provide any DNA concentration. There is no discussion or suggestion anywhere in Yguerabide of a nanoparticle having any recognition and/or diluent oligonucleotides and/or particle surface density. The claims recite limitations that are neither taught, made obvious, or suggested by the cited reference. Thus, the Applicant respectfully submits that Yguerabide cannot be applied to support section 102(e) and/or section 103(a) rejections of the claims.

In conclusion, the Applicants respectfully submit that the claims in this application are in allowable condition and request a Notice to this effect.

Reconsideration of this application is respectfully requested and a favorable determination is earnestly solicited. The Examiner is invited to contact the undersigned

representative if the Examiner believes that this would be helpful in expediting the prosecution of this application.

Dated: 6-18-03

Respectfully submitted,



Emily Miao  
Reg. No. 35,285

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## APPENDIX A

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
00-653-A	U.S. 09/927,777 Filed 8/10/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton, Garamella, Li, Park/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERE TO AND USES THEREFORE	PENDING
00-713-B1	09/923,625 Filed 8/7/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERE TO AND USES THEREFOR	PENDING
00-713-C	09/344,667, filed 6/25/99	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERE TO AND USES THEREFORE	U.S. Patent No. 6,361,944, issued 3/26/02
00-713-I	U.S.S.N 09/603,830 Filed 6/26/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton; NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERE TO AND USES THEREFOR	U.S. Patent No. 6,506,564, issued 1/14/03
00-713-I-1	09/961,949 9/20/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton;	U.S. Patent No. 6,582,921, issued June 24, 2003

<b>ATTY Case No.</b>	<b>Serial No./ Filing Date</b>	<b>Inventors/Title</b>	<b>Status</b>
		NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERE TO AND USES THEREFOR	
<b>00-713-I-2</b>	09/957,318 9/20/01	See 00-713-I-1	PENDING
<b>00-713-I-3</b>	09/957,313 9/20/01	See 00-713-I-1	ALLOWED
<b>00-713-I-4</b>	09/966,491 9/28/01	See 00-713-I-1	ALLOWED
<b>00-713-I-5</b>	09/966,312 9/28/01	See 00-713-I-1	ALLOWED
<b>00-713-I-6</b>	09/967,409 9/28/01	See 00-713-I-1	PENDING
<b>00-713-I-7</b>	09/974,500 10/10/01	See 00-713-I-1	PENDING
<b>00-713-I-8</b>	09/974,007 10/10/01	See 00-713-I-1	PENDING
<b>00-713-I-9</b>	09/973,638 10/10/01	See 00-713-I-1	PENDING
<b>00-713-I-10</b>	09/973,788 10/10/01	See 00-713-I-1	PENDING
<b>00-713-I-11</b>	09/975,062 10/11/01	See 00-713-I-1	PENDING
<b>00-713-I-12</b>	09/975,376 10/11/01	See 00-713-I-1	PENDING
<b>00-713-I-13</b>	09/975,384 10/11/01	See 00-713-I-1	PENDING
<b>00-713-I-14</b>	09/975,498 10/11/01	See 00-713-I-1	ALLOWED

<b>ATTY Case No.</b>	<b>Serial No./ Filing Date</b>	<b>Inventors/Title</b>	<b>Status</b>
<b>00-713-I-15</b>	09/975,059 11/11/01	See 00-713-I-1	PENDING
<b>00-713-I-16</b>	09/976,601 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I-17</b>	09/976,968 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I-18</b>	09/976,971 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I-19</b>	09/976,863 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I-20</b>	09/976,577 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I-21</b>	09/976,618 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I-22</b>	09/981,344 10/15/01	See 00-713-I-1	PENDING
<b>00-713-I-23</b>	09/976,900 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I-24</b>	09/976,617 10/12/01	See 00-713-I-1	PENDING
<b>00-713-I-25</b>	09/976,378 10/12/01	See 00-713-I-1	PENDING
<b>00-713-i-26</b>	TBA 041003	See 00-713-I-1	PENDING
<b>00-713-L</b>	U.S.S.N. 09/693,005 Filed 10/20/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERETO AND	U.S. Patent No. 6,495,324, issued 12/17/02

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
		USES THEREFORE	
00-713-M	U.S.S.N. 09/693,352 Filed 10/20/00	Mirkin, Letsinger, Mucic, Storhoff, Elghanian/ NANOPARTICLES HAVING OLIGONUCLEOTI DES ATTACHED THERE TO AND USES THEREFORE	U.S. Patent No. 6,417,340, issued 7/9/02
00-714-G	U.S. 09/830,620 Filed 8/15/01	Mirkin, Nguyen/ NANOPARTICLES WITH POLYMER SHELLS	PENDING
00-715-A	U.S. 09/760,500 Filed 1/12/01	Mirkin, Letsinger, Mucic, Storhoff, Elghanian, Taton; Garamella, Li/ METHOD OF ATTACHING OLIGONUCLEOTI DES TO NANOPARTICLES AND PRODUCTS PRODUCED THEREBY	PENDING
00-1085-A	U.S.S.N. 09/820,279 Filed 3/28/01	Mirkin, Letsinger, etc./ METHOD AND MATERIALS FOR ASSAYING BIOLOGICAL MATERIALS	ALLOWED
00-1086-A	U.S. 09/903,461 Filed 7/11/01	Letsinger, Garimella/ METHOD OF DETECTION BY ENHANCEMENT OF SILVER STAINING	ALLOWED
01-565-A	USSN 10/125,194 Filed 4/18/02	Mirkin, Nguyen, Watson, Park/ OLIGONUCLEOTI DE-MODIFIED ROMP POLYMERS AND CO-	PENDING

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
		POLYMERS	
01-599-A	U.S.S.N. 10/291,291 Filed 11/08/02	Storhoff/NOVEL THIOL-BASED METHOD FOR ATTACHING OLIGONUCLEOTI DES TO NANOPARTICLES	PENDING
01-661-A	U.S.S.N. 10/034,451 Filed 12/28/01	Mirkin, Cao, Jin/ DNA-MODIFIED CORE-SHELL AG/AU NANOCRYSTALS	PENDING
01-661-C	U.S.S.N. 10/153,483 Filed 5/22/02	Mirkin, Cao, Jin/ DNA-MODIFIED CORE-SHELL AG/AU NANOCRYSTALS	PENDING
01-1565-A	U.S.S.N. 10/266,983 Filed 10/08/02	Park, Taton, Mirkin/ARRAY- BASED ELECTRICAL DETECTION OF DNA USING NANOPARTICLE PROBES	PENDING
01-1705-A	U.S.S.N. 10/108,211 Filed 3/27/02	Nam, Park, Mirkin/BIO- BARCODES BASED ON OLIGONUCLEOTI DE-MODIFIED NANOPARTICLES	PENDING
02-338-B	USSN 10/172,428 Filed 6/14/02	Cao, Jin, Nam, Mirkin/MULTI- CHANNEL DETECTION USING NANOPARTICLE PROBES WITH RAMAN SPECTROSCOPIC FINGERPRINTS	PENDING
02-338-C	TO BE ASSIGNED	Cao, Jin, Nam, Mirkin/MULTI- CHANNEL DETECTION	PENDING



June 18, 2003

Page 6 of 6

ATTY Case No.	Serial No./ Filing Date	Inventors/Title	Status
	5/7/03	NNEL DETECTION USING NANOPARTICLE PROBES WITH RAMAN SPECTROSCOPIC FINGERPRINTS	

FORM PTO-1449  
(Rev. 2-32)

U.S. Department of Commerce  
Patent and Trademark Office

Atty. Docket No.

Serial No.

00-713-48

09/974,007

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

(Use several sheets if necessary)

Applicant:

Chad A. Mirkin, et al.

Filing Date:

October 10, 2001

Group:

1637

U.S. PATENT DOCUMENTS

Examiner Initial		Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	1.	4,996,143	02/26/91	Heller, et al.	435	6	04/13/90
	2.	5,508,164	04/16/96	Kausch, et al.	435	6	10/29/93
	3.	5,922,537	07/13/99	Ewart, et al.	435	6	11/8/96
	4.	5,972,615	10/26/99	An, et al.	435	6	01/21/98
	5.	6,264,825	07/24/01	Blackburn, et al.	205	777.5	06/23/99
	6.	6,214,560	04/10/01	Yguerabide, et al.	435	7.1	04/18/97

FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Subclass	Translation Yes No	
	7.	WO 94/29484	12/22/94	PCT				
	8.	WO 00/25136	05/04/00	PCT				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	9.	Mohanty J., et al. "Pulsed laser excitation of phosphate stabilized silver nanoparticles," <i>Proc. Indian Acad. Sci.</i> , Vol. 112, No. 1, p. 63-72.
	10.	Peña-Nicewarner S., et al., "Hybridization and Enzymatic Extension of Au Nanoparticle-Bound Oligonucleotides," <i>J. Am. Chem. Soc.</i> , Vol. 124, p. 7314-7323 (2002)
	11.	Whitesides G.M., et al., "Soft Lithography in Biology and Biochemistry," <i>Annu. Rev. Biomed. Eng.</i> , p. 335-373 (2001)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication.



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Hon. Commissioner of  
Patents and Trademarks

S/N—09/974,007

Atty EM

Re: Applicant - Mirkin, et al.

Case No. 00-713-i8

**Nanoparticles Having Oligonucleotides Attached Thereto and Uses Therefor  
VIA HAND DELIVERY TO EXAMINER JEZIA RILEY, GROUP ART UNIT 1637**

Sir:

Please place the Patent Office receipt stamp hereon and mail to acknowledge receipt of:

- ☒ Transmittal Letter
- ☒ Sixth Supplemental Information Disclosure Statement
- ☒ U.S. PTO 1449 Form with copies of 29 references

**Binders IX-XI**

**Fee Enclosed**

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Respectfully,

McDonnell Boehnen Hulst & Berghoff  
Attorney for Applicant

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## PATENT

**For: NANOPARTICLES HAVING  
OLIGONUCLEOTIDES ATTACHED  
THERE TO AND USES THEREFOR**

**Confirmation No. 8209**

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## **SIXTH SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

In order to comply with discretionary regulations 37 CFR §§1.97 and 1.98, attached hereto is Form PTO-1449, copies<sup>1</sup> of the documents listed thereon: These documents contain information which the Examiner may consider to be important in deciding whether to allow the present application to issue as a patent.

1. Merrill, et al., U.S. Patent No. 5,830,986, issued November 3, 1998.
2. Lough, et al., U.S. Patent No. 5,900,481, issued May 4, 1999.

<sup>1</sup>To the extent that a document is listed and no copy of same is attached, then such document is not at the present time available to the undersigned or is available in the file of a parent application. If a listed document is not in the English language and an English translation is readily available, such translation is also attached; if translation is not attached it is not readily available to the undersigned. If a foreign language patent document is cited, and an English language equivalent is known to the undersigned, then such equivalent patent is also cited on the attached form along with the corresponding foreign language patent and a connecting arrow indicated therebetween; if no such English language equivalent is cited, then none is known to undersigned.

3. Goldberg, et al., U.S. Patent No. 6,203,989, issued March 20, 2001
4. Bawendi, et al., U.S. Patent No. 6,251,303, issued June 26, 2001.
5. Abbott, et al., U.S. Patent No. 6,277,489, issued August 21, 2001.
6. Bawendi, et al., U.S. Patent No. 6,306,610, issued October 23, 2001
7. Mirkin, et al, U.S. Patent No. 6,361,944, issued March 26, 2002.
8. Wagner, et al., U.S. Patent No. 6,365,418, issued April 02, 2002
9. Mirkin, et al., U.S. Patent No. 6,417,340, issued July 09, 2002
10. WO 93/25709 published 23 December 1993.
11. WO 98/04740 published 5 January 1998
12. WO 98/17317 published 30 April 1998
13. WO 99/60169 published 25 November 1999
14. WO 00/33079 published 8 June 2002
15. WO 01/00876 published 4 January 2001
16. WO 01/51665 published 19 July 2001
17. WO 01/73123 published 4 October 2001
18. WO 01/86301 published 15 November 2001
19. WO 02/04681 published 17 January 2002
20. WO 02/18643 published 7 March 2002
21. WO 02/36169 published 10 May 2002
22. WO 02/46483 published 13 June 2002
23. WO 02/46472 published 13 June 2002.
24. Letsinger, R., et al., "Chemistry of Oligonucleotide-Gold Nanoparticle Conjugates," *Phosphorus, Sulfur and Silicon*, Volume 144, p. 359-362 (1999)

25. Letsinger, R., et al., "Use of a Steroid Cyclic Disulfide Anchor in Constructing Gold Nanoparticle—Oligonucleotide Conjugates," *Bioconjugate Chem*, p. 289-291 (2000)
26. Li Z., et al., "Multiple thiol-anchor capped DNA-gold nanoparticle conjugates," *Nucleic Acids Research*, Volume 30, p. 1558-1562 (2002)
27. Nuzzo R., et al., "Spontaneously Organized Molecular Assemblies. 3. Preparation and Properties of Solution Adsorbed Monolayers of Organic Disulfides on Gold Surfaces," *J. Am Chem. Soc.*, Volume 109, p. 2358-2368 (1987)
28. Otsuka, H, et al., "Quantitative and Reversible Lectin-Induced Association of Gold Nanoparticles Modified with  $\alpha$ -Lactosyl- $\omega$ -mercapto-poly(ethyleneglycol)," *J. Am Chem. Soc.*, Volume 123, p. 8226-8230 (2001).
29. Wuelfing, P, et al, "Nanometer Gold Clusters Protected by Surface-Bound Monolayers of Thiolated Poly(ethylene glycol) Polymer Electrolyte," *J. Am. Chem. Soc.*, Volume 120, p. 12696-12697 (1998)

In accordance with MPEP Sections 609 and 707.05(b), it is requested that each document cited (including any cited in applicant's specification which is not repeated on the attached Form PTO-1449) be given thorough consideration and that it be cited of record in the prosecution history of the present application by initialing on Form PTO-1449. Such initialing is requested even if the Examiner does not consider a cited document to be sufficiently pertinent to use in a rejection, or otherwise does not consider it to be prior art for any reason, or even if the Examiner does not believe that the guidelines for citation have been fully complied with. This is requested so that each document becomes listed on the face of the patent issuing on the present application.

The present Disclosure Statement is being submitted in compliance with 37 CFR 1.56 insofar as an Examiner might consider any of the cited documents important in deciding whether to allow the application to issue as a patent, but the citation of each document is not to be construed as an admission that such document is necessarily relevant or prior art. No representation is intended

that the cited documents represent the results of a complete search, and it is anticipated that the Examiner, in the normal course of examination, will make an independent search and will determine the best prior art consistent with 37 CFR 1.104(a) and 1.106(b) and, in the course of each search, will review for relevance every document cited on the attached form even if not initialed.

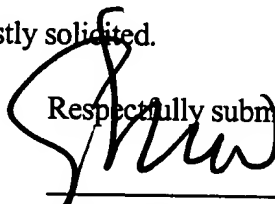
Early and favorable consideration is earnestly solicited.

Dated: \_\_\_\_\_

9/6/02

McDonnell Bochen Hulbert & Berghoff  
300 South Wacker Drive  
Chicago, Illinois 60606  
Telephone : (312) 913-0001  
Facsimile: (312) 913-0002

Respectfully submitted,



Emily Miao  
Registration No. 35,285



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JUL 09 2003

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Hon. Commissioner of S/N—09/974,007

Patents and Trademarks

Atty EM

Re: Applicant - Mirkin, et al.

Case No. 00-713-i8

Nanoparticles Having Oligonucleotides Attached Thereto and Uses Therefor  
Date Mailed:

Sir:

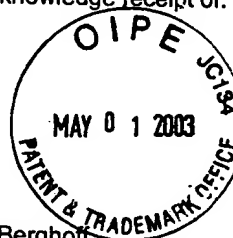
Please place the Patent Office receipt stamp hereon and mail to acknowledge receipt of:

- ☒ Transmittal Letter
- ☒ Seventh Supplemental Information Disclosure Statement
- ☒ U.S. PTO 1449 Form with copies of 11 references

Fee Enclosed

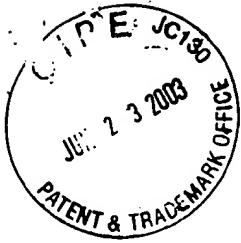
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Respectfully,  
McDonnell Boehnen Hulbert & Berghoff  
Attorney for Applicant



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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
(Case No. 00-713-i8)

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In the Application of:

Chad A. Mirkin, et al.

Serial No.: 09/974,007

Filed: October 10, 2001

For: NANOPARTICLES HAVING  
OLIGONUCLEOTIDES ATTACHED  
THERETO AND USES THEREFOR

Examiner: Jezia Riley

Group Art Unit: 1637

Confirmation No.: 8209

Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

**SEVENTH SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

Sir:

In order to comply with discretionary regulations 37 CFR §§1.97 and 1.98, attached hereto is Form PTO-1449, copies<sup>1</sup> of the documents listed thereon. These documents contain information which the Examiner may consider to be important in deciding whether to allow the present application to issue as a patent.

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2. Kausch, et al., U.S. Patent No. 5,508,164 issued 04/16/96
3. Ewart, et al., U.S. Patent No. 5,922,537 issued 07/13/99
4. An, et al., U.S. Patent No. 5,972,615 issued 10/26/99

<sup>1</sup>To the extent that a document is listed and no copy of same is attached, then such document is not at the present time available to the undersigned or is available in the file of a parent application. If a listed document is not in the English language and an English translation is readily available, such translation is also attached; if translation is not attached it is not readily available to the undersigned. If a foreign language patent document is cited, and an English language equivalent is known to the undersigned, then such equivalent patent is also cited on the attached form along with the corresponding foreign language patent and a connecting arrow indicated there between; if no such English language equivalent is cited, then none is known to undersigned.

5. Blackburn, et al., U.S. Patent No. 6,264,825 issued 07/24/01
6. Yguerabide, et al., U.S. Patent No. 6,214,560 issued 04/10/01
7. International Patent WO 94/29484 published 12/22/94
8. International Patent WO 00/25136 published 05/04/00
9. Mohanty J., et al., "Pulsed laser excitation of phosphate stabilized silver nanoparticles," *Proc. Indian Acad.*, Vol. 112, No. 1, p. 63-72 (2000)
10. Nicewarner- Peña S., et al., "Hybridization and Enzymatic Extension of Au Nanoparticle-Bound Oligonucleotides," *J. Am. Chem. Soc.*, Vol. 124, p. 7314-7323 (2002)
11. Whitesides G.M., et al., "Soft Lithography in Biology and Biochemistry," *Annu. Rev. Biomed. Eng.*, p. 335-373 (2001)

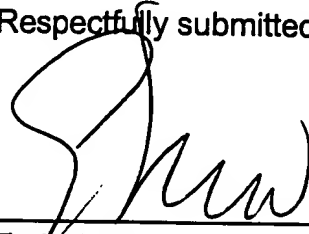
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of examination, will make an independent search and will determine the best prior art consistent with 37 CFR 1.104(a) and 1.106(b) and, in the course of each search, will review for relevance every document cited on the attached form even if not initialed.

Early and favorable consideration is earnestly solicited.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Emily Miao', written over a horizontal line.

Emily Miao  
Registration No. 35,285

Dated: 5-1-03

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